NEUROPEPTIDES IN LEARNING AND MEMORY PROCESSES, D. De Wied, Department of Medical Pharmacology, Rudolf Magnus Institute for Neurosciences, Utrecht University, Universiteitsweg 100, 3584 CG Utrecht, The Netherlands.

Neuropeptides are generated following gene expression in nerve cells and produced in large precursor molecules which are processed in biologically active peptides. The cascade of cell specific processes which express the genetic information determine the quantity and quality of the peptides synthesized. In this way neuropeptides with different, sometimes opposite and more selective properties are formed from the same precursor. Since the seventies, numerous peptides have been discovered in the brain. Time- and dose-dependent postlearning effects, modification of neuronal excitability, the presence of these neuropeptides and their receptors in brain structures in particular involved in information processing (cortex, hippocampus, amygdala, thalamus), greater effectiveness following intracranial treatment, and disturbances in learning and memory following immunoneutralization, gene- or receptor blockade are essential criteria for a neuropeptide to be involved in cognition per se. Vasopressin and oxytocin meet these criteria. Both neurohormones are converted in the brain into C-terminal fragments (AVP/OXT 4-9, 4-8) which are stronger acting and more selective on avoidance behavior. The active core of ACTH/MSH peptides on avoidance behavior is located in the sequences ACTH 4-7 and 7-16. Such peptides might be generated from ACTH/MSH in the brain. Structure activity studies with peptides related to ACTH/MSH led to the synthesis of a highly selective ACTH 4-9 analog (ORG 2766) devoid of inherent endocrine activities and a markedly increased potency on avoidance behavior. It appeared to be much more resistant towards enzymatic degradation and orally active. Most neuropeptides have context-specific effects. Vasopressin, for example has the most robust effect in fear-motivated behavioral test situations, while the effects of CCK, NPY and galanin are most prominent in food-motivated behavior, oxytocin, LHRH, and ACTH/MSH peptides in sexual components of learning (Kovács and De Wied, Pharmacol. Rev. 46, 269-291, 1994). A substantial number of studies with ACTH/MSH neuropeptides in particular with Org 2766, and with AVP, DDAVP and DGAVP in patients with cognitive disturbances as a result of head trauma, dementia e.o. revealed modest effects on cognition and social behavior in a number of subjects. Modest effects were also found in healthy volunteers.

Source: https://www.industrydocuments.ucsf.edu/docs/lgcb0000